

To - Directors of Public Health of PCTs & Medical Directors of NHS Trusts:

Please ensure that this message is also cascaded to anaesthetists and surgeons

MESSAGE FROM PROFESSOR SIR GORDON DUFF, CHAIRMAN OF THE COMMISSION ON HUMAN MEDICINES

CEM/CMO/2007/21

APROTININ - SUSPENSION OF MARKETING DUE TO SAFETY CONCERNS

5 November 2007

Dear Colleague,

I am writing to inform you that the UK licence holders for aprotinin (Trasylol), Bayer and Nordic Pharma, have today voluntarily suspended global marketing following the termination of a clinical trial suggesting that aprotinin may be associated with an increased risk of death compared with tranexamic acid and aminocaproic acid.

New advice on practice

Aprotinin should only be used after careful consideration in individual cases where, for example, the risk of blood loss during surgery is considered to be particularly high (e.g. redo CABG surgery), where there is no suitable alternative, and only when the likely benefits outweigh any risks to individual patients.

Background

The indication for aprotinin was restricted in 2006 to the prevention of major blood loss during coronary artery bypass graft surgery in patients at high risk of bleeding. This followed evidence that aprotinin was associated with a risk of renal failure.

Evidence has emerged over the last 2 years suggesting that aprotinin may also be associated with an increased risk of cardiac and cerebral disorders, as well as all-cause mortality. As these data were derived from observational studies, we have been awaiting data from a randomised clinical trial (the BART study) before taking any further action. The BART study has now been terminated due to a possible excess number of deaths in patients being treated with aprotinin compared with patients treated with aminocaproic acid

or tranexamic acid. This was despite evidence from the trial that aprotinin was associated with less serious bleeding (including bleeding severe enough to require re-operation) than the other two drugs.

The BART study was conducted by independent researchers, and very little further information from this study is currently available. The preliminary data suggest that the excess mortality had not yet reached statistical significance, but there was an evident trend throughout the study. Until the full data are available, the companies have made the precautionary decision to suspend the marketing of aprotinin.

Next steps

A full regulatory review of the balance of risks and benefits of aprotinin is underway. The outcome of this depends on availability of data from the BART study and this may take at least 3 months. The Commission on Human Medicines (CHM) will be considering the current position at its meeting this week.

Any further advice will be issued as soon as available. For further information please contact the Medicines and Healthcare products Regulatory Agency (MHRA) at 020 7084 2000 (www.mhra.gov.uk).

Professor Sir Gordon Duff
Chairman, Commission on Human Medicines